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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/253,573	02/19/1999	HAI XING CHEN	99.001	5784

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/15/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/253,573	CHEN, HAI XING	
	Examiner	Art Unit	
	Richard Schnizer	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-21 and 24-43* is/are pending in the application.

4a) Of the above claim(s) *30-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-21 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

An amendment was received and entered as Paper No. 16 on 4/25/021. Claims 9, 22, and 23 were canceled as requested. Claims 1-8, 10-21, and 24-43 are pending. Claims 30-43 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6. Claims 1-8, 10-21, and 24-29 are under consideration in this Office Action.

K.T. 9/14

Claim Objections

Claims 1-8, 10-21, and 24-29 stand objected to because they lack an article preceding the words "blood stream". It is also noted that "blood stream" should be condensed into a single word.

Rejections Withdrawn

The rejections of claims 1-5, 8, 16-19, and 25-27 under 35 USC 102, and of claims 1, 6, 7, 16, 20, and 21 under 35 USC 103, are withdrawn. While the Hollis reference teaches that red blood cell precursors may be transfected with expression vectors for the purpose of producing and purifying, without secretion, recombinant proteins, this reference does not teach that this particular embodiment of the invention should be practiced in vivo. Statements regarding the production of recombinant proteins in vivo are made in the context of cells modified to produce

and secrete recombinant proteins. For this reason the instant claim limitation requiring rupture of the red blood cells for release of the produced protein renders the claims novel and non-obvious over the art of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-8, 10-21, and 24-29 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record in Paper No. 14.

The claimed invention is a method for producing and delivering protein *in vivo*. Claims 1-8 and 10-15 comprise delivering to progenitors of mammalian red blood cells isolated from a mammalian host an expression construct comprising a promoter operably linked to a gene encoding a protein which is not native to red blood cells. The transfected progenitors are then reintroduced into the mammalian host, wherein they give rise to red blood cells containing the desired protein. The red blood cells subsequently lyse, resulting in delivery of the protein. Lysis

may be induced by genetic mutation. Claims 16-21 and 24-29 are similar to claims 1-8 and 10-15 except that the promoter must be a hemoglobin promoter

The asserted use of the invention is the delivery of therapeutic proteins. See page 10, lines 13-15; page 11, lines 10-20; page 13, lines 7-24; page 14, line 4 to page 16, line 1. The specification discloses that the claimed invention "has a broad scope of applications in treating diseases". See page 14, lines 4 and 5. Specific diseases which may be treated using the claimed invention including cystic fibrosis, Duchenne muscular dystrophy, hemophilia A, Huntington's disease, familial hypercholesterolemia, fragile-X syndrome, and cancer in general. See page 14, lines 12-15 and paragraph bridging pages 14 and 15. The specification also considers treating diseases in general through the delivery of enzymes and hormones. See page 14, lines 15-30. **The specification asserts no use for producing and delivering protein *in vivo* other than for the treatment of disease.** For these reasons, in order to enable the invention for its intended use, the specification must teach how to use the invention for the treatment of the range of diseases set forth in the specification.

A review of the prior art shows that techniques for isolating, transfecting and successfully engrafting red blood cell precursors were established at the time of the invention. See US Patent 5,665,350, *e.g.* claims 2 and 4-6. It is also clear that this technique could be used to produce the encoded proteins. See e.g. Plavec et al (Blood 81(5):1384-1392, 3/1993), abstract. However, obtaining sufficient expression of proteins for therapeutic purposes is problematic. At the time the invention was made, successful implementation of gene therapy protocols was not routinely

obtainable by those skilled in the art. This is reflected by several review articles. Orkin (Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy, 1995) teaches that "significant problems remain in all basic aspects of gene therapy. Major difficulties at the basic level include shortcomings in all current transfer vectors and an inadequate understanding of the biological interaction of these vectors with the host" (page 1, item 3). Orkin teaches that problems exist in delivering nucleic acid sequences to the appropriate target cell or tissue and achieving the appropriate level of expression within that cell or tissue (page 9). Verma et al (Nature 389: 239-242, 1997) teach that "there is still no single outcome that we can point to as a success story (p. 239, col 1). The authors state further, "Thus far, the problem has been the inability to deliver genes efficiently and to obtain sustained expression" (p.239, col. 3). Anderson (Nature 392:25-30, 1998) confirms the unpredictable state of the art, stating that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human disease" (p. 25, col. 1) and concluding, "Several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered" (p.30). The instant specification acknowledges the unpredictability of the art at page 1, lines 11-19, which indicates that "no approach has definitively improved the health of one of the more than 2,000 patients who have enrolled in gene therapy trials worldwide."

Claims 16-21 and 24-29 require the use of a hemoglobin promoter to drive expression of the selected gene. Persons et al reviewed the history of attempted therapy of hemoglobin

disorders by *ex vivo* transfection and reimplantation of red blood cell precursors. See Proc. Nat Acad. Sci. USA 97(10):5022-5024, 5/2000). This article emphasizes the difficulty in obtaining globin promoter-driven expression of proteins in red blood cell precursors, specifically citing problems with gene silencing and position effect variegation. See entire document especially paragraph bridging columns 1 and 2 on page 5022; column 2, line 21 through first full paragraph in column 3, page 5022. Thus prior to, and subsequent to, the time the invention was filed, those of skill in the art were unable to obtain therapeutic concentrations of proteins within red blood cells using globin promoters. The claimed invention requires delivery of proteins after lysis of red blood cells, thus the problem of poor expression of protein is compounded by the problem of dilution into the blood stream. This necessarily lowers the concentration of the proteins and points to a need for far higher efficiency of expression than that obtained using globin promoters, because the specification fails to teach any method of targeting proteins to any specific tissue. The claimed mode of delivery also fails to account for the biology of some of the disorders it is intended to treat. For example, the specification teaches treatment of cystic fibrosis by supply of a desired protein. See page 14, lines 4-15. Cystic fibrosis is caused by a defective version of a transmembrane ion transporter, the cystic fibrosis transmembrane conductance regulator (CFTR), and the effect of the disease is manifested in the lungs. Certainly one could not expect to deliver a functional CFTR and expect it to spontaneously integrate into the appropriate alveolar membrane without the aid of a ribosome and from the extracellular side of the membrane.

However, the specification provides no guidance or examples as to how one of skill in the art could treat this loss function by delivery through the blood of any desired protein.

The specification fails to identify specific proteins which should be used to treat a variety of the diseases which are asserted to be treatable with the instant invention, such as Huntington's disease, Gaucher's disease, familial hypercholesterolemia, and cystic fibrosis. Furthermore the specification fails to give any guidance whatsoever as to how much of any specific gene product would be required to treat any given disease, or how to obtain any specific dosage or administration profile. It fails to teach how many cells should be delivered for any given treatment or how to protect released proteins from proteases present in the blood.

Claims 10 and 24, require that the rupture of red blood cells containing the expressed protein must be induced by genetic mutation of these cells. The specification fails to disclose a single example of any such mutation nor any guidance whatsoever as to what mutations will afford such an effect. Because these mutations are required by the claim, they must be considered to be critical elements of the invention. While Applicant is not required to disclose that which is well known in the art, there is an obligation to disclose critical elements of the invention as well as how to use these elements. In Genentech, Inc, v Novo Nordisk A/S, the court found that when the specification omits any specific starting material required to practice an invention, or the conditions under which a process can be carried out, there is a failure to meet the enablement requirement. See 42 USPQ2d 1001.

> It is true, as Genentech argues, that a specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94

> (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

In this case, the identification of specific genes used to treat specific diseases, dosages of cells, expression profiles required to effect treatment, and mutations which induce lysis of red blood cells cannot be considered minor details which can be omitted in the process of providing an enabling disclosure.

The claims also require that the expressed protein must be contained only in red blood cells. The specification describes a red blood cell as one which has no nucleus, thus the term red blood cell is understood by the PTO to refer to mature red blood cells. However the prior art teaches that proteins present in red blood cells, particularly those expressed from globin promoters, are expressed at all stages of erythroid cell differentiation. See e.g. Kim et al (Blood 47(5):767-776, 5/1976), abstract. Neither the prior art of record nor the specification provide any guidance or examples as to how to delay translation of mRNA until developing erythrocytes reach maturity. Thus one of skill in the art could not practice the invention as claimed.

Because the specification fails to teach how to treat any specific disease through the use of the claimed invention, much less the variety of diseases disclosed, because the prior art shows that gene therapy was highly unpredictable at the time of the invention, and because the

specification fails to disclose mutations which can induce lysis of red blood cells or how to use them in the invention, one of skill in the art could not use the invention as intended by the specification, without undue experimentation.

Response to Arguments

Applicant's arguments filed 4/25/02 have been fully considered but they are not persuasive.

Applicant's response to the rejection extends from page 8 to page 13 of Paper No. 16. At page 8 Applicant reviews the prosecution history with respect to enablement. At page 9, first paragraph Applicant reiterates the position that the claimed invention is a method of in vivo protein production and delivery, asserting that although the invention may be used for disease treatment, it is not intended to be a specific gene therapy protocol. This raises the question of for what, other than gene therapy, the invention is intended to be used. At page 11 of the response Applicant argues that the specification teaches a host of utilities, citing page 6 of the specification. The cited utilities include "a non-tissue specific method for the synthesis of proteins; a means to control the expression and production of proteins in the precursors of red blood cells; taking advantage of the lack of a nucleus in a red blood cell to provide enhanced stability of proteins after their production; bypassing exocytosis and secretion pathways for protein release; and using a hemoglobin promoter to control expression of proteins in red blood cell precursors. None of these utilities provides reason for the in vivo production and delivery of

proteins as claimed. The Examiner has carefully read the specification and found that, as stated in the rejection above, the specification asserts no use for the production and delivery of proteins in vivo other than therapy. Because of this, in order to adequately teach how to use the invention for the purpose for which it is intended, the specification must enable the practice of gene therapy of the broad range of diseases set forth in the specification.

At paragraph 4 of page 9, Applicant argues that they are not required to provide enablement for gene therapy because it is a separate invention. In response, the Office reiterates that Applicant must teach how to use the invention for the purpose for which it was intended to be used. The specification discloses no use for the invention other than gene therapy, so in order to enable the claimed invention the specification must teach how to perform gene therapy. It does not, for the reasons set forth above.

In the paragraph bridging pages 9 and 10, Applicant asserts that the claimed invention may be viewed as a process which produces a product (gene therapy), and argues that the process is separate from the product. In support of this position Applicant draws an analogy to a method of producing time-release capsules for vitamin C, arguing that they would not be responsible for the clinical use of vitamin C. This is unpersuasive for two reasons. First Applicant's logic regarding enablement and the relationship between a product and a process of using it is flawed. If the use of a product is not enabled, then a method for making that product is cannot be enabled unless it can be used to make some other useful product. Second, the analogy is improper because one of skill in the art can clearly use vitamin C, therefore a method of

delivering it in vivo can be enabled. In the instant case, the specification fails to teach how to produce and deliver proteins for the intended therapeutic purpose.

At page 10 of the response Applicant argues that in vivo protein delivery and expression are enabled as evidenced by the Hollis reference used in rejections under 35 USC 102. This is unpersuasive because Hollis recites the utility of producing recombinant proteins for a purpose other than gene therapy, i.e. purification. See column 8, lines 18-24. The instant specification recites no such use, and the instant claims require "delivering a protein in vivo". This is clearly distinct from the asserted use of Hollis limited to production of the recombinant protein for non-therapeutic use, i.e. purification.

Applicant's argues at paragraph 4 of page 10 that the Examiner agreed in the first Office Action that the invention was enabling for delivery of a protein in vivo. This is irrelevant because that position was withdrawn after further consideration. The standing rejection cites no such scope of enablement, and is proper in view of the intended use of the invention as set forth in the specification.

At page 11, paragraph three Applicant argues that it would be unjust to require applicant to delay seeking patent protection on a mechanism of protein delivery until after "the specific gene therapy has been discovered and proven. This is unpersuasive for the reasons set forth above, i.e. enablement of the claims depends on whether the specification teaches how to make and use the invention. In this case the only asserted use of the invention is in gene therapy. For

this reason, the specification must enable the use of the invention in gene therapy. The specification fails to do this for the reasons given above.

At pages 11-13 of the response Applicant further considers the enablement of claims 10 and 24. Applicant argues at paragraph 3 of page 12 that they need not make available genes which would be required for the practice of the invention, because the genes are well known in the art. In response, the Office reiterates that, because the genes are required to practice the invention, they must be considered to be critical elements of the invention. As noted above, the failure to disclose critical elements of an invention results in a failure to meet the enablement requirement, regardless of whether or not the material was known in the prior art. See Genentech, Inc, v Novo Nordisk A/S, 42 USPQ2d 1001. Secondly, none of the references provided by Applicant disclose the precise nature of any of the mutations which could be used for this purpose, *i.e.* the nucleotide sequences which would be required in order to practice the invention are not disclosed, thus one of skill in the art would be required to determine empirically which mutations give the desired effect. Applicant has failed to show that the required mutated genes are not critical elements of the claimed invention, and has failed to show why the findings of the court are in error. Third, it is noted that almost all of the mutations disclosed are recessive in nature, and Applicant has not taught how these mutations could be used in cells which also express the corresponding wild type gene. In the presence of one or more wild type alleles, these mutant genes would have no effect. Thus the specification fails to teach the conditions under which the process can be carried out, and there is a failure to meet the

enablement requirement. Fourth, the problems with sustained gene expression which currently cripple the art of gene therapy would also apply in this case, and in particular to the only dominant mutation disclosed in the references. Applicant has not taught what level of gene expression is required in order to achieve the lytic effect, how to obtain this level of expression, or how to sustain it long enough to get the required effect. Thus, even if the lysis-inducing mutations were not critical elements of the invention, the specification and the prior art still fail to teach one of skill in the art how to use them within the context of the invention. Finally, Applicant has failed to make available any of these mutations, or cells comprising them, and has provided no guidance whatsoever in the process of generating such mutations or cells. Applicant's response to these issues appears to be limited to a statement in paragraph 4 of page 12 indicating that known genetic techniques can be used to practice the invention. As stated above, both the specification and the art at the time of the invention failed to teach what level of gene expression was required to obtain lysis of red blood cells, or how to obtain this level of expression. Applicant has provided no evidence or reasoning to the contrary.

For these reasons the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-5, 13, 15-21 and 24-29 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record in Paper No. 14.

Claims 3 and 18 are indefinite because it is unclear what is intended by "natural promoter". Although this phrase is defined at page 8, lines 9 and 10 as "the promoter present in the gene of a protein that is native to the cell", cellular nucleic acids are continually evolving, their sequences are constantly changing. Thus one of skill in the art could not know which promoter sequences were embraced by the claims at the time of the invention.

Claims 4 and 19 are indefinite because they recite the term "mutated", which is a relative term that modifies the term "promoter". Neither the claims nor the specification set forth any standard reference "wild type" promoter against which one could compare another promoter in order to determine if it is "mutated". Furthermore, it is unclear if the use of the term mutated refers to a change in nucleotide sequence relative to a reference sequence, or whether the mutation must result in an assayable phenotype, and if so, what phenotype. Thus one of skill in the art cannot know which promoters are embraced by the claims.

Claim 5 is confusing because it refers to promoters which are native to red blood cells. As noted at page 11, line 3 of the specification, red blood cells comprise no nucleus, so there are no promoters which are native to red blood cells.

Claims 13 and 27 are indefinite because it is unclear what are the metes and bounds of the genus of "naturally-occurring" proteins. Because proteins are continually evolving, their sequences are constantly changing. Thus one of skill in the art could not know which protein sequences were embraced by the claims at the time of the invention.

Claims 15 and 29 are indefinite because they recite the term "mutated", which is a relative term that modifies the term "protein". Neither the claims nor the specification set forth any standard reference "wild type" protein against which one could compare another protein in order to determine if it is "mutated". Furthermore, it is unclear if the use of the term mutated refers to a change in amino acid sequence relative to a reference sequence, or whether the mutation must result in an assayable phenotype, and if so, what phenotype. Thus one of skill in the art cannot know which proteins are embraced by the claims.

Claims 16-21 and 24-29 are indefinite because they require a "hemoglobin promoter". There is no such thing as a hemoglobin promoter in the context of mammalian cells, and the specification fails to define the term. Hemoglobin is a tetrameric protein complex comprising for separate polypeptides of two different types. In adults, hemoglobin is composed of two alpha chains and two beta chains. The alpha and beta chains are encoded by separate genes on separate chromosomes under the control of separate promoters with distinct functional characteristics. See for example, Voet et al, page 1142, column 2, first sentence of first full paragraph, and Humphries et al (Cell 30(1): 173-183, 8/1982), abstract. A search for the term "hemoglobin promoter" in the Medline database yielded only three hits, and these each referred to plant

hemoglobin. Thus "hemoglobin promoter" is a term of art only in the context of plants, and not in the context of the instant invention.

Response to Arguments

Applicant's arguments filed 4/25/02 have been fully considered but they are not persuasive.

Applicant addresses the rejections at pages 13-15 of the response. At page 14 Applicant argues that the term natural promoter is defined in the specification in a manner consistent with that exemplified by Hollis at column 2, lines 54-63. This is unpersuasive because neither of these definitions clearly delineates the metes and bounds of the instant claims. Neither of these definitions allows one of skill in the art to determine which promoter sequences were members of the genus of "natural" promoters at the time of the invention, and which were not.

Applicant argues at paragraph 3 of page 14 that the claims are not indefinite because they are not unreasonably uncertain in light of the prior art and the specification, relying for support on In re Tanksley. This is unpersuasive because Applicant has not shown that the claims are not unreasonably uncertain. For example, Applicant has failed to explain how one of skill in the art would be able to determine which sequences are natural and which are not because no basis for comparison was provided. Because sequences are constantly evolving, the genus of natural sequences is constantly changing. What is construed as a non-natural sequence today could arise

from a natural source tomorrow. Thus one of skill in the art could not know the metes and bounds of the invention.

Applicant has not responded to specifically to the rejection of claims 16-21 and 24-29 over the term "hemoglobin promoter".

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This application contains claims **30-43** drawn to an invention nonelected with traverse in a telephone conversation with Yi Li on 6/15/99. A complete reply to the final rejection must

include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014. Additionally correspondence can be transmitted to the following RIGHTFAX numbers: 703-872-9306 for correspondence before final rejection, and 703-872-9307 for correspondence after final rejection.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.

JAMES KETTER
PRIMARY EXAMINER